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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/258,132	02/26/1999	PHILIP GOELET	04990.0007.U	3407

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David A. Kalow, Esq.
KALOW, SPRINGUT & BRESSLER, LLP
488 Madison Ave.
19th Floor
New York, NY 10022

EXAMINER

MYERS, CARLA J

ART UNIT PAPER NUMBER

1634

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/258,132

Applicant(s)

GOELET ET AL.

Examiner

Carla Myers

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 October 2004 and 25 October 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 64 and 66-71 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 64 and 66-71 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 10/18/04, 10/25/04
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/14/04 has been entered.

Claims 64 and 66-71 are pending. This action contains a new grounds of rejection and is made non-final.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 64, 66, 67, and 69-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen et al (EP 0412883A1 (published February 13, 1991; cited in the IDS) or Cohen et al (FR 2,650,840 (published February 15, 1991; cited in the IDS), each in view of Davis (WO) 90/11372, October 4, 1990; cited in the IDS).

It is noted that EP 0412883A1 claims priority to application 8910802, which issued as and is identical in content to FR 2,650,840. An English translation of FR 2,650,840 was filed in the IDS of June 8, 1999.

Cohen teaches a method for determining the identity of one or more nucleotide bases in a nucleic acid molecule wherein the method comprises contacting a single-stranded nucleic acid sample with an oligonucleotide primer to form a duplex between the primer and complementary target nucleic acids present in the sample, wherein the primer hybridizes immediately 3' of the nucleotide to be determined; contacting the duplexes with a solution containing four different terminators, each terminator labeled with a different detectable moiety; extending the primer with the terminator, and determining the identity of the incorporated terminator to thereby determine the identity of the nucleotide base (see pages 4 and 5). Cohen (page 6) states that "if the four blocking bases are marked by means of different markers, the four blocking nucleotides are advantageously detected at the same time." In the method of Cohen, only terminator nucleotides are present in the extension reaction – the reaction does not contain dATP, dCTP, dGTP or dTTP (see, for instance, Example 1). Cohen does not

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teach using performing the primer extension reaction using multiple primers, each comprising a different affinity moiety.

However, Davis teaches a method for determining the identity of one or more nucleotide bases in a nucleic acid molecule wherein the method comprises contacting a single stranded nucleic acid molecule with an oligonucleotide primer to form a duplex between the primer and complementary target nucleic acids; contacting the duplexes with a solution containing labeled dNTPs, labeled with a different detectable moiety; extending the primer with the dNTPs such that if the primer is perfectly complementary with the target nucleic acid, an extension product is formed, but if the primer contains a mismatch at or near the 3' end of the primer, an extension product is not formed, and detecting the presence of an extension product in order to determine the identity of a nucleotide base (see pages 3-4). Davis teaches that the identity of multiple nucleotides can be determined simultaneously by using a mixture of different oligonucleotides, each oligonucleotide comprising a unique tail (i.e., affinity moiety). Following the extension reaction, the primer extension/target nucleic acid complex is denatured, and the primer extension product is hybridized to a solid support having bound thereto sequences complementary to the primer tail. The unique tail allows for the primers to be immobilized at specific locations on the support (see pages 4-5). Davis teaches that the use of multiple primers, with different tail sequences allows for the simultaneous analysis of multiple sequences and improves the speed and sensitivity of the detection method (see page 21).

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Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Cohen so as to have used multiple primers, each having a different tail (i.e., each comprising a different affinity moiety) and to have separated the primer extension products from the reaction medium by contacting the extension products with a solid support having immobilized thereon a capture probe complementary to the tail sequence (i.e., an affinity group complementary to the affinity moiety of the primer) in order to have accomplished the objectives set forth by Davis of allowing for the analysis of multiple sequences simultaneously and of providing a more rapid and sensitive means for determining the identity of a nucleotide.

With respect to claim 66, Cohen teaches that the terminator (or "blocking nucleotide") is a dideoxynucleotide (see page 5). With respect to claim 67, Cohen teaches that the terminator comprises one or more of ddATP, ddCTP, ddGTP or ddTTP (see pages 7 and 8). With respect to claims 69 and 70, Cohen teaches that the terminator may be labeled with a fluorophore, or chromophore, isotope, enzyme or antibody (see page 5).

3. Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen et al (EP 0412883A1 (published February 13, 1991; cited in the IDS) or Cohen et al (FR 2,650,840 (published February 15, 1991; cited in the IDS), each in view of Davis (WO 90/11372, October 4, 1990; cited in the IDS) and Prober (U.S. Patent NO. 5,332,666).

The teachings of Cohen and Davis are presented above. The combined references do not teach using a terminator that comprises arabinoside triphosphate.

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However, Prober teaches methods for determining a nucleotide sequence wherein the method comprises performing a primer extension reaction using a terminator. Prober teaches that the terminator may contain an arabinose as the sugar group and provides a number of examples of terminators comprising an arabinoside triphosphate (see column 18).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Cohen so as to have a terminator comprising an arabinoside triphosphate because this would have provided an equally effective terminator for the extension reaction and for determining the identity of a nucleotide in a target nucleic acid.

4. Claim 71 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cohen et al (EP 0412883A1 (published February 13, 1991; cited in the IDS) or Cohen et al (FR 2,650,840 (published February 15, 1991; cited in the IDS), each in view of Davis (WO 90/11372, October 4, 1990; cited in the IDS) and Tabor (U.S. Patent NO. 4,962,020; cited in the IDS).

The teachings of Cohen and Davis are presented above. The combined references do not teach including pyrophosphatase in the primer extension medium.

However, Tabor (columns 15-16) teaches including pyrophosphatase in primer extension reactions. The reference teaches that pyrophosphatase removes pyrophosphate which builds up during extension reactions. Specifically, Tabor (column 14) teaches that in the presence of pyrophosphate, DNA polymerase will add pyrophosphate to the 3' terminal nucleotide, causing the release of dideoxynucleoside

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5'-triphosphates. As stated by Tabor (column 15, lines 1-2), "This reaction has the effect of removing the block at the 3' terminus."

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Cohen so as to have included pyrophosphatase in the reaction medium in order to have achieved the expected benefit of eliminating pyrophosphorolysis activity of DNA polymerase and thereby reducing the probability that the labeled terminator would be removed and that unlabeled dideoxynucleotides would be released into the reaction medium. Thereby, the ordinary artisan would have been motivated to have include pyrophosphatase in the extension reaction in order to have ensured the accuracy and sensitivity of the method for determining the identity of a nucleotide.

5. It is noted that in parent application 07/664,837, a declaration was filed under 37 CFR 1.131 establishing conception and reduction to practice of a method for determining the identity of a nucleotide using a primer extension reaction incorporating labeled dideoxynucleotides as of April 1990. However, affidavits or declarations, such as those under 37 CFR 1.131, filed during prosecution of the parent application do not automatically become a part of any continuing application. Where it is desired to rely on an earlier filed affidavit or declaration, the applicant should make the remarks of record in the later application and include a copy of the original affidavit or declaration filed in the parent application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach

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the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Carla Myers
November 22, 2004


CARLA J. MYERS
PRIMARY EXAMINER